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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,692	01/11/2002	Thomas R. Cech	015389-002640US	3439

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EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/044,692	CECH ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *71-74,76,77 and 79-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *71-74,76,77 and 79-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/18/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed July 18, 2007 is acknowledged and has been entered. Claims 25, 75, 78 have been cancelled and new claims 79-82 have been added. An action on the RCE follows.

2 Claims 71-74, 76-77, 79-82 are pending and currently under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4, The following rejections are being maintained:

Claim Rejections - 35 USC 112

5. Claims 74, 76-77 remain rejected and newly added claims 80, 82 are rejected under 35 USC 112, first paragraph essentially for the reasons previously set forth in the paper mailed January 18, 2007, Section 4, pgs 2-6.

Applicant argues that the fragments disclosed by the inventors are not "undefined", rather the polypeptides are defined by SEQ ID NO:2 and that provided with SEQ ID NO:2 and the teachings of the specification, one of skill would immediately envision the hTRT fragments.

The argument has been considered but has not been found persuasive because contrary to Applicant's arguments although one would immediately envision fragments of SEQ ID NO:2 one would not immediately envision immunogenic fragments that will elicit an adaptive immune response against SEQ ID NO:2, and as previously set forth, the immunogenic fragments of at least ten

contiguous amino acids of SEQ ID NO:2 that will elicit an adaptive immune response against SEQ ID NO:2 when administered to a subject are undefined as the specification provides no guidance or information drawn to the fragments that will function as claimed. Further, the fragments "comprising" are clearly undefined because it is not possible to determine the structures of those fragments "comprising" or to determine the effect of additional amino acids on the immunogenicity of the claimed fragments comprising.

Applicant argues that there is a clear correlation between the structure of the fragments and their function and if as Examiner acknowledges, one of skill would immediately envision that the full length sequence will elicit an adaptive immune response against SEQ ID NO:2, Applicant's believe it beyond dispute that one of skill would also envision that hTRT fragments will elicit an immune response against SEQ ID NO:2, more particularly, an hTRT fragment corresponding to a particular region of the hTRT protein (i.e. a particular amino acid sequence) will elicit an immune response to epitopes located in the particular region.

The argument has been considered but has not been found persuasive because the art recognizes the unpredictability of identifying immunogenic fragments within a full length polypeptide as well as the unpredictability of the elicitation of antibodies against linear peptides that will in fact bind to the full length antigen. Thus contrary to Applicant's arguments, although an hTRT SEQ ID NO:2 fragment might elicit an immune response to epitopes located in the fragment, it cannot be predicted that the immune response will be specific for/bind to SEQ ID NO:2. In particular, Roitt et al (Immunology, 1993, Mosby, St. Louis, p 7.7-7.8) teach that although it is possible to produce antibodies to almost any part of an antigen, this does not normally happen in an immune response. It is

usually found that only certain areas of the antigen are particularly antigenic, and that a majority of antibodies bind to these regions. These regions are often at exposed areas on the outside of the antigen, particularly where there are loops of polypeptide that lack a rigid tertiary structure (p.7.7-7.8). This is exemplified by the teaching of Holmes (Exp. Opin.Invest. Drugs, 2001, 10(3):511-519) who teaches that rabbits were immunized with synthetic peptides which in each case generated high anti-peptide specific immunoreactivities, however, none of the antibodies exhibited binding to the full length antigen. The author concludes that 'Presumably, expression of these epitopes in the context of the protein was important and affected the antibody binding ability' (p. 513, col 1). Furthermore, it is noted that the specification does not take into account the 3 dimensional folding of the native molecule, nor its glycosylation or other post-translational modifications and other characteristics which are of significant importance in an antibody response. Peptides or synthetic antigens cannot effectively substitute for the natural tertiary and quarterary structure of a protein in a physiological situation.

In addition, there is no teaching in the specification of whether or not the epitopes within SEQ ID NO:2 are linear or comprise 3-dimensional structures. In particular, Greenspan et al (Nature Biotechnology, 1999, 7:936-937) teaches that defining epitopes is not as easy as it seems. Even when the epitope is defined, in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (page 937, 2nd column) and Flower (Trends in Immunology, 2003, 24: 667-674) teaches that the accurate prediction of epitopes to which the antibody would bind is difficult and the complexity of immunogenic epitopes continually confounds efforts at prediction, see p. 667, right column.

Given the above, in the absence of any guidance correlating the structure of the claimed fragments to the function of eliciting an immune response against SEQ ID NO:2, that is that will bind to and recognize SEQ ID NO:2, it is clear that the written description of the claimed invention is not adequate and does not meet the standard of 35 USC 112, first paragraph.

Applicant argues that the Office has previously argued that "all molecules will elicit an immune response [to themselves] under appropriate circumstances" and argue that given Examiner's argument, since hTRT fragments are molecules that will elicit an immune response to themselves, they will also elicit an immune response to corresponding epitopes on full-length hTRT. Applicant opines that this is understood by biologists with undergraduate level training and would certainly have been recognized by those of ordinary skill in the biomedical arts.

The argument has been considered but has not been found persuasive because although a biologist with only an undergraduate level of training might believe that fragments of an antigen will reliably and predictably produce an immune response not only to themselves but also to corresponding epitopes on a full length polypeptide, certainly no one of ordinary skill in the art would believe it more likely than not that fragments of an antigen will reliably and predictably produce an immune response not only to themselves but also to corresponding epitopes on a full length polypeptide as clearly disclosed by those of ordinary skill who have written the cited references above.

Applicant argues that the recitation of the limitation that the encoded polypeptides comprises at least 10 contiguous amino acids of SEQ ID NO:2 elicits an adaptive immune response against SEQ ID NO:2 overcomes the previous rejection.

The argument has been considered but has not been found persuasive to overcome the rejection under the Written Description Guidelines because although the "comprising" claims now recite the limitation that the immune response is against SEQ ID NO:2, the art recognizes, as clearly taught by Holmes et al, Supra, that expression of these epitopes in the context of the protein was important and affected the antibody binding ability'. Clearly the corollary is true, that is, that if the epitope is not in the context of the native antigen structure, it would be expected that this alteration would affect the ability of the fragment to elicit an antibody that will bind to the native protein because the structure of epitope within the polypeptide "comprising" would not be the same as the structure of the fragment within the context of the native protein. Thus, it cannot be predicted that an antigenic epitope that is not in the context of the native antigen will in fact elicit antibodies that bind to the native antigen.

Applicant concludes that those of skill would clearly recognize the inventor's possession of the claimed subject matter and points to a reference that refers to Applicant's contribution to the art. The argument has been considered but has not been found persuasive because the specification provides no information drawn to the amino acid residues critical to the immunogenic fragments that will function as claimed and in the absence of this teaching, the specification is simply naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of and this is not a description of that material. Given that the specification does not provide adequate written description of the claimed invention that meets the standard of 35 USC 112, first paragraph written description, it is clear that the specification has failed to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The arguments have been considered but have not been found persuasive and the rejection is maintained.

6. Claim 73 remains rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed January 18, 2007, Section 8, pages 7-8.

Applicant acknowledges that Applicant cannot pick and chose unrelated elements from a specification and combine them to result in a combination never contemplated in the specification, but argues that the law permits combining related elements in a specification to craft a particular claim. In the present case, the entire specification is focused on compositions and uses related to a particular protein and Applicant opines that one of skill in the art would find nexus between descriptions of hTRT and uses of hTRT in various parts of the specification.

Applicant argues that one of ordinary skill would recognized that the inventors had possession of an hTRT polypeptide with at least 98% identity to SEQ ID NO:2 that elicits an immune response to hTRT and further argues that the specification teaches that an immune response can be elicited by administration of naked DNA, that the invention provides a wide variety of hTRT proteins useful in the induction of an anti-TRT immune response (wherein applicant specifically points to p. 37 lines 3-14 which indicate that the wide variety of hTRT proteins are useful for a wide variety of applications which are not limited, as suggested by applicant, to the induction of an anti-TRT immune response) wherein the specification teaches sequences that have substantial identity to the polynucleotide encoding SEQ ID NO:2 which include 98% identity (at paragraph 0476 of the published application), wherein one of skill in the art would have recognized that

polypeptides with substantial sequence identity to the hTRT protein of SEQ ID NO:2 could be used to induce an immune response, wherein the specification recites that peptides used to induce specific antibodies typically have an amino acid sequence consisting of .....at least 10 amino acids.....of SEQ ID NO:2.

The argument has been considered but has not been found persuasive because the section drawn to percent identity is not drawn to the production of an immune response and nothing in that section points to any nexus or even a contemplation of "A composition containing a nucleic acid that encodes a polypeptide comprising a sequence at least 98% identical to the 1132 residues of SEQ. ID NO:2, wherein the composition elicits an adaptive immune response against hTRT (SEQ. ID NO:2) when administered to a subject." as currently claimed. Thus, it is clear that everything that Applicant's arguments support Examiner's finding that the newly added limitations represent new matter. Applicant's arguments make clear that Applicant is picking and choosing unrelated elements from the specification to combine them to result in a combination never contemplated in the specification. Further, it is noted that arguments drawn to "at least 10 amino acids.....of SEQ ID NO:2" are not convincing given that the claim as currently constituted is not drawn to peptides comprising at least 10 amino acids.

The arguments have been carefully considered but have not been found persuasive and the rejection is maintained.

Double Patenting

7. Claims 71-74, 76-77 remain rejected and newly added claims 79-82 are rejected under the provisions of obviousness-type Double Patenting for the reasons previously set forth in the paper mailed January 18, 2007, Section 6, pg 6.

Applicant argues that the rejection of the claims over US Patent No. 6,261,636 should be revisited in light of the response filed November 10, 2005. Upon review of the response, the rejection of the claims over US Patent No. 6,261,636 is hereby withdrawn.

As drawn to the rejection of the claims over US Patent No. 6,261,836, this rejection is maintained and Applicant states that Applicant will provide a terminal disclaimer or otherwise respond to this rejection upon indication that the claims are otherwise allowable. The rejection stands.

New Grounds of Rejection

Claim Rejections - 35 USC 112

8. Claims 71-74, 76-77, 79-82 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 71-74, 76-77, 79-82 are indefinite in the recitation of the term "adaptive immune response". Neither the claims nor the specification define the term and given that http://www.answers.com/topic/adaptive defines the term adaptive as meaning "Relating to or exhibiting adaptation" , wherein adaptation is biologically defined as "An alteration or adjustment in structure or habits, often hereditary, by which a species or individual improves its condition in relationship to its environment" or physiologically as "The responsive adjustment of a sense organ, such as the eye, to varying conditions, such as light intensity" and given that an immune response does not appear to fit into any of these definitions, the metes and bounds of the claimed patent protection cannot be determined from the information in the specification or in the claims as currently constituted.

9. No claims allowed.

10. All other objections and rejections set forth in the previous office action are hereby withdrawn.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Ungar
Primary Patent Examiner
September 6, 2007